EFFECTS OF AOM INJECTION AND RESISTANT STARCH CONSUMPTION ON THE INHIBITION OF COLORECTAL CARCINOGENESIS IN AN A/J MOUSE MODEL

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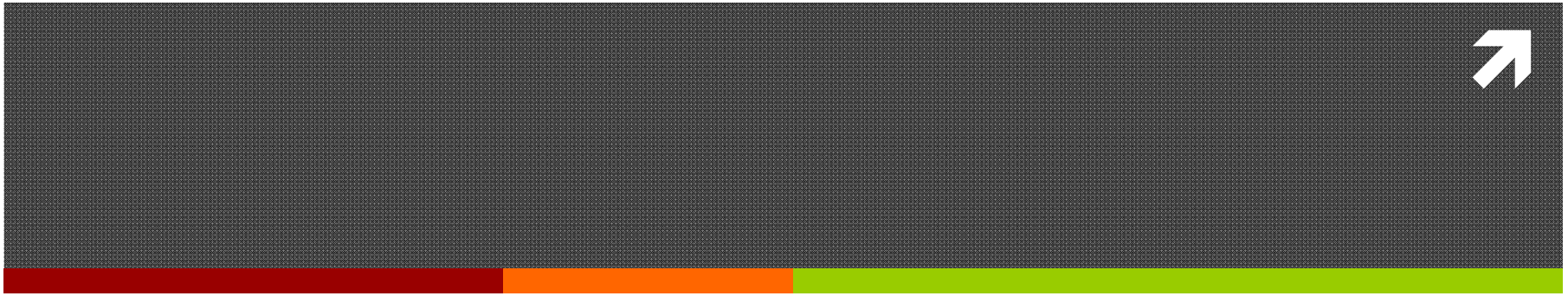
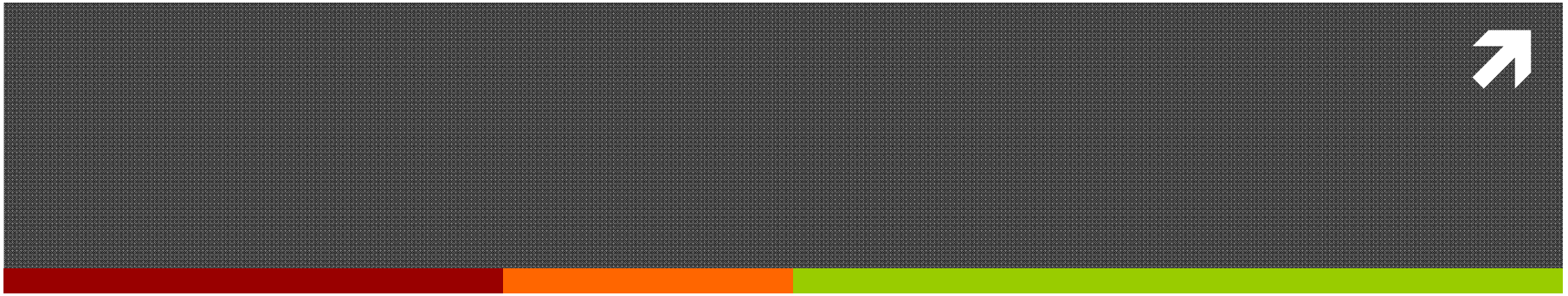
OUTLINE

- Background
- Purpose
- Hypothesis
- Methods
- Results
- Discussion



COLORECTAL CANCER

- Third most prevalent cancer among both males and females
    - 108,000 new diagnoses each year
- Effect of diet on Colorectal Cancer
    - Fiber can inhibit carcinogenesis
- Risk factors: obesity, inactivity, red meat consumption, smoking



AZOXYMETHANE (AOM)

- Carcinogen used to induce colonic tumors
- Correct dosage of 7.5 mg/kg body weight was validated in previous study
- Mice receive injections prior to experimental diets
  - Prevents diet interference with AOM metabolism

RESISTANT STARCH (RS)

- Type of fiber that escapes normal digestion in the small intestine
    - Available for fermentation in the colon that is hypothesized to decrease carcinogenesis through tumor inhibition

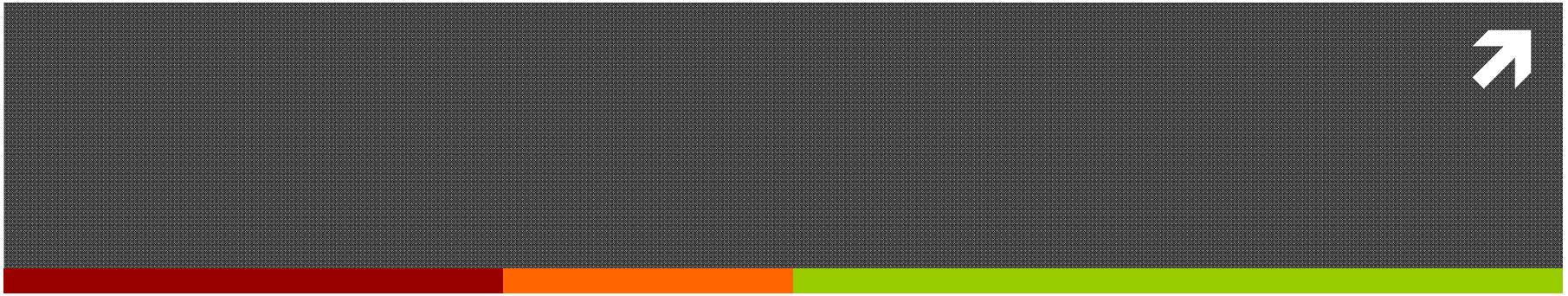
- Types of Resistant Starch
    - RS1 – Grains
    - RS2 – Bananas
    - RS3 – Potatoes and Rice
    - RS4 – Chemically modified
    - RS5 – SA-complexed

PURPOSE

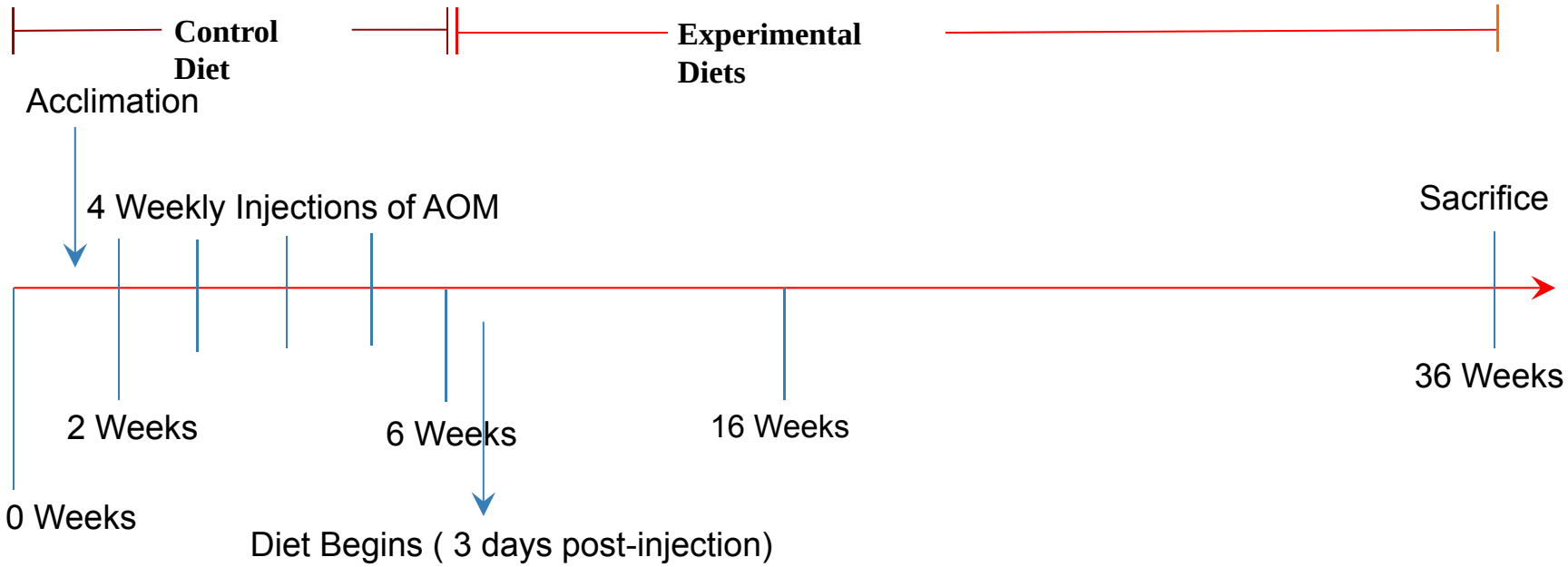
- To study the effects of two resistant starch diets (HA7 and RS5) in an A/J mouse model injected with Azoxymethane (AOM) compared to a saline control (corn starch) on the inhibition of carcinogenesis within the colon and rectum

HYPOTHESIS

- We hypothesize that a positive correlation will exist between the resistant content of the starch and the inhibition of carcinogenesis.
- Rationale: A higher resistant content allows for more fermentation in the large intestine → protective effect against colorectal cancer



STUDY TIMELINE

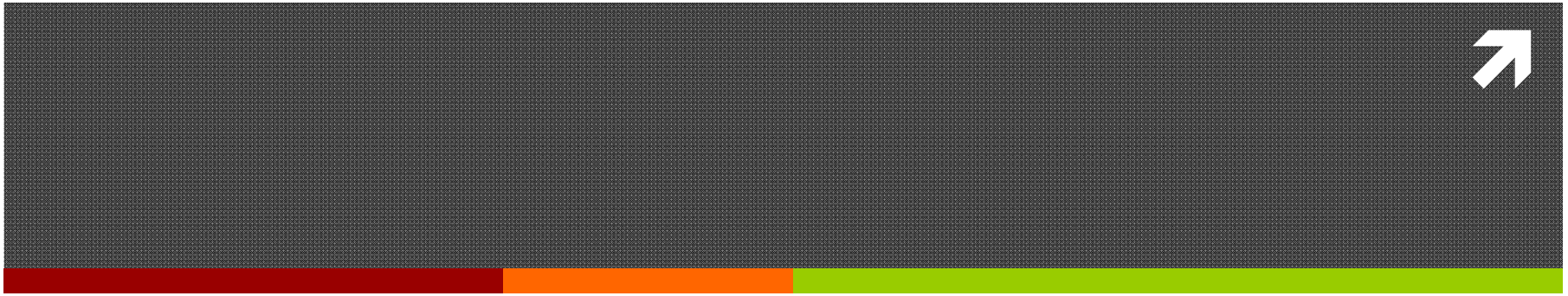


METHODS- VARIOUS Diets

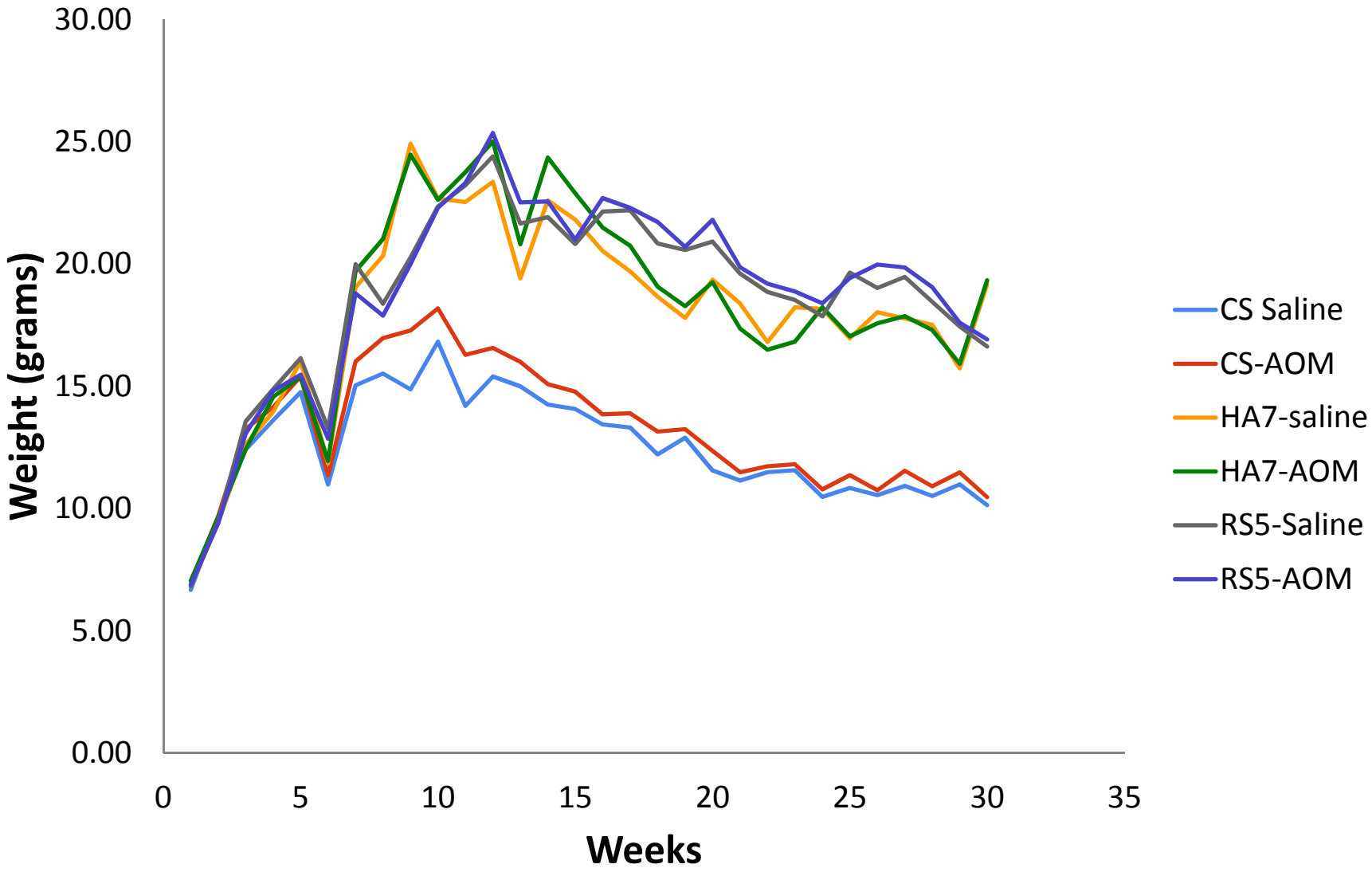
Saline Originally assigned: n=10	AOM Originally assigned: n=30
Control Starch n=9	Control Starch n=27
HA7 n=9	HA7 n=29
RS5 n=9	RS5 n=29

Diet Groups

- Control
  - Commercially available corn starch (negligible)
- HA7
  - High-amylose type 7 corn starch (25.9%)
- RS5
  - Resistant starch type 5, aka SA-HA7 (59.1%)



Food Disappearance Data



Food Disappearance Discussion

1.) The initial climb in food disappearance peaks at INJ week 3 where it then declines through INJ week 4

- likely cause: stress

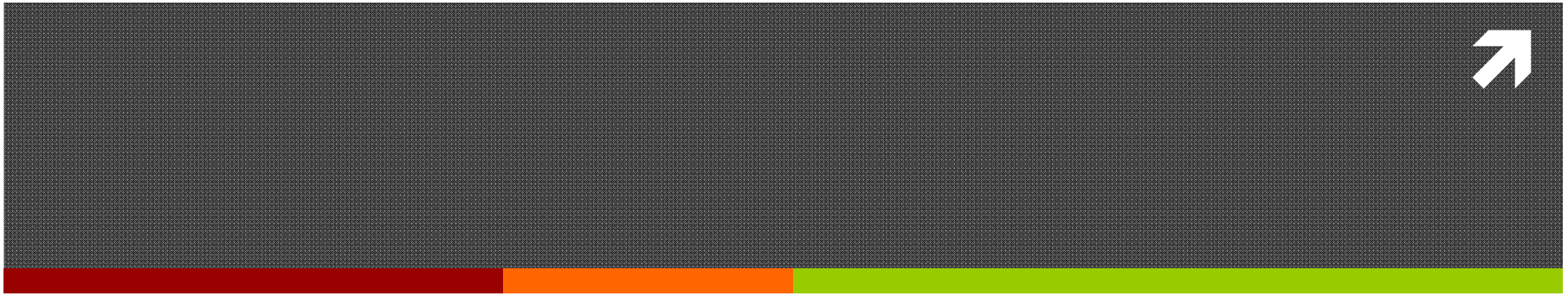
2.) Post INJ week 4: increase in food disappearance

- assumption: stress from injections is short-lived

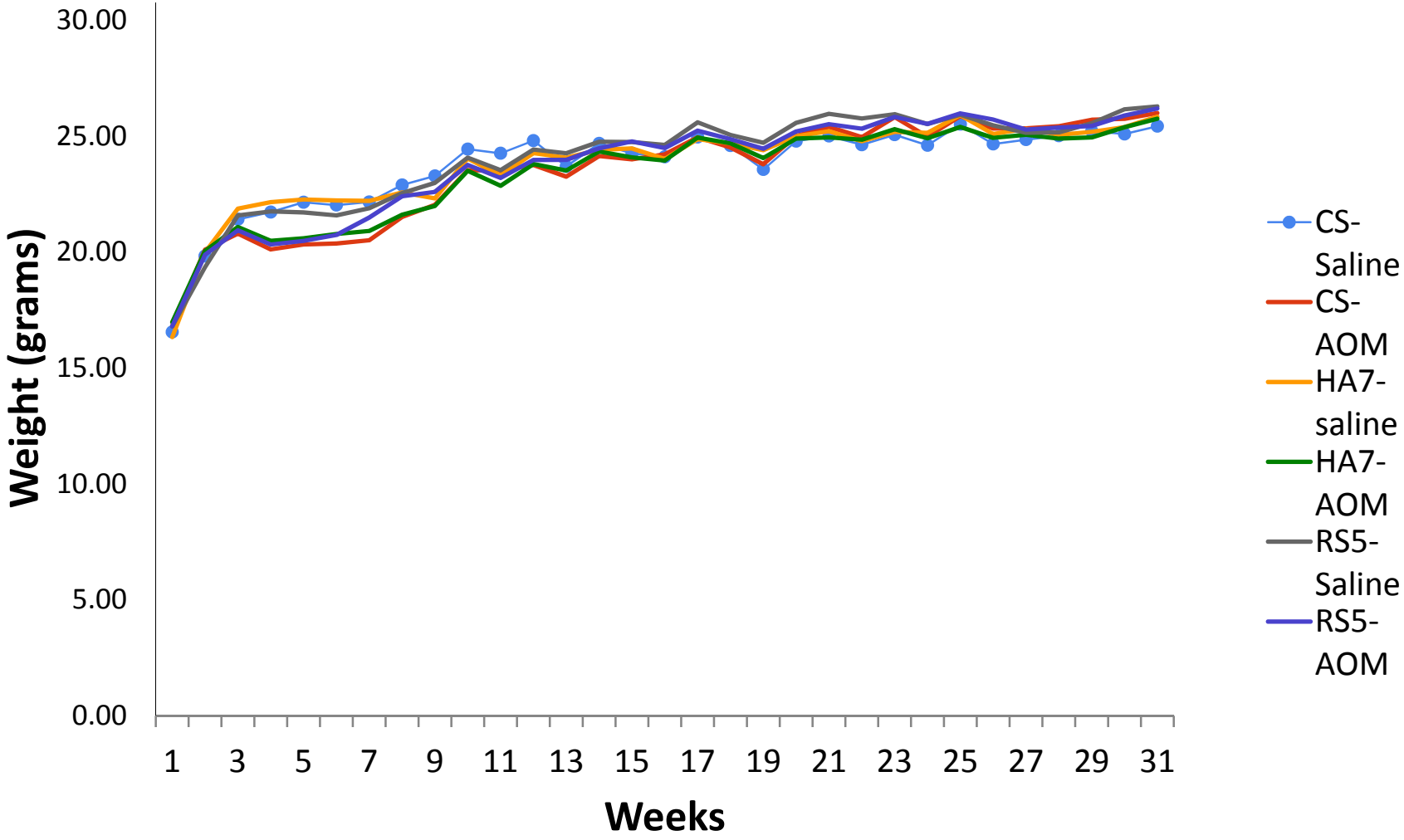
3.) Branching: HA7 and RS5 diet groups show the greatest degree of food disappearance

-due to diet consistency

4.) No significant differences observed between Saline and AOM treated groups



BODY WEIGHT


30.00
25.00
20.00
15.00
10.00
5.00
0.00
Weight (grams)
1
3
5
7
9
11
13
15
17
19
21
23
25
27
29
31
Weeks
CS-Saline
CS-AOM
HA7-saline
HA7-AOM
RS5-Saline
RS5-AOM

BODY WEIGHT DISCUSSION

1.) No major observable differences between diet or treatment groups

2.) AOM impacts body weight during injections: greater stress→ less consumption→ lower BW

- Mice are able to rebound after: short-term stressor

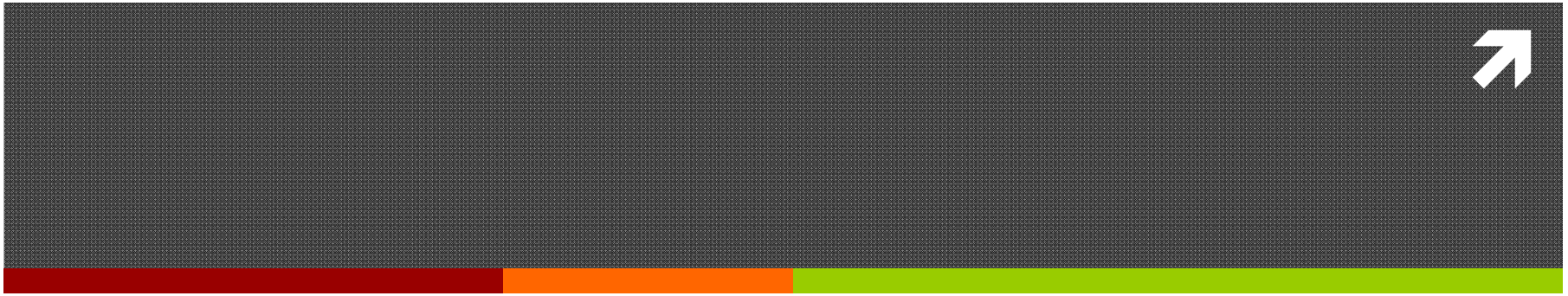
3) Body weights began to plateau at week 20 of the study

4) Body weights are predicted to decrease with progressions of carcinogenesis

HEALTH SUMMARY

- Mice appear to have declining health consistent with stress and aging
  - Excessive barbering has led to a scruffy appearance

- 2 Control AOM and 1 RS5 Saline were euthanized due to gross observation



Discussion End Points

- HA7 and RS5 are sustainable for life and appear to be palatable
- Body weight is predicted to decrease once tumors have begun to form
- Food disappearance still gradually declining

WHAT'S LEFT IN THIS STUDY?

- Study will conclude in 5 weeks
- Mice will be sacrificed
- Colons and rectums will be extracted for analysis
- Tumors and preneoplasia by histopathology
- Completion of study will support or refute our hypothesis

ACKNOWLEDGEMENTS

Dr. Diane Birt

Dr. Elizabeth Whitley

Nicole Cray

Bridget Nelson

Nidhi Shah